

# Obesity – surgical treatment and molecular mechanisms

## Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademien, Göteborgs Universitet, kommer att offentligen försvaras i Sahlgrenska Aula, Sahlgrenska Universitetssjukhuset, Blå Stråket 5, Göteborg, torsdagen den 3 december kl. 13:00

av

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Fakultetsopponent:

Professor Tommy Olsson

Institutionen för folkhälsa och klinisk medicin

Umeå Universitet, Umeå

Avhandlingen baseras på följande arbeten:

- I. **Evaluation of current eligibility criteria for bariatric surgery: diabetes prevention and risk factor changes in the Swedish obese subjects (SOS) study.** Sjöholm K, Anveden Å, Peltonen M, Jacobson P, Romeo S, Svensson PA, Sjöström L, Carlsson LM. *Diabetes care*, 2013. 36(5): p. 1335-40.
- II. **Alcohol consumption and alcohol problems after bariatric surgery in the Swedish obese subjects study.** Svensson PA, Anveden Å, Romeo S, Peltonen M, Ahlin S, Burza MA, Carlsson B, Jacobson P, Lindroos AK, Lönroth H, Maglio C, Näslund I, Sjöholm K, Wedel H, Söderpalm B, Sjöström L, Carlsson LM. *Obesity*, 2013. 21(12): p. 2444-51.
- III. **Cancer incidence up to 26 years after bariatric surgery – results from the Swedish obese subjects study.** Anveden Å, Peltonen M, Jacobson P, Andersson-Assarsson J, Taube M, Sjöholm K, Sjöström L, Svensson PA, Carlsson LM. *Manuscript*.
- IV. **ITIH-5 expression in human adipose tissue is increased in obesity.** Anveden Å, Sjöholm K, Jacobson P, Palsdottir V, Walley AJ, Froguel P, Al-Daghri N, McTernan PG, Mejhert N, Arner P, Sjöström L, Carlsson LM, Svensson PA. *Obesity*, 2012. 20(4): p. 708-14



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# Obesity – surgical treatment and molecular mechanisms

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## ABSTRACT

Obesity is a condition of high prevalence and is associated with increased morbidity and mortality. Bariatric surgery is an effective treatment of obesity and reduces the risk for morbidity and mortality, but little is known of who would benefit the most from this treatment as well as of potential long-term side effects. Furthermore, there is a need for increased understanding of the molecular mechanisms in the adipose tissue and its association with obesity and morbidity.

The overall aim of this thesis was to increase our understanding on how obesity is associated with disease through molecular mechanisms, and to explore effects of bariatric surgery on different outcomes in different subgroups, as well as exploring potential side effects. Specific aims were to compare the effects of bariatric surgery on type 2 diabetes incidence and cardiovascular risk factors in subjects eligible and non-eligible for surgery according to today's eligibility criteria, to explore whether bariatric surgery is associated with increased incidence of alcohol use disorders, to explore the effects of bariatric surgery on overall cancer incidence, as well as specific cancers and groups of cancers, and to investigate the gene and protein expression of the *ITIH5* gene in different adipose tissue depots and its association with obesity.

Long-term effects of bariatric surgery have been assessed using the Swedish obese subjects (SOS) study, which is a prospective, controlled, intervention study. Outcomes have been evaluated using the SOS study follow-up examinations and questionnaires, as well as by cross-checking social security numbers with the Swedish Cancer Registry and the Swedish National Patient Register. The association between *ITIH5* adipose tissue expression and obesity has been investigated in different study cohorts, using different methods for gene and protein expression.

Bariatric surgery was found to have a protective effect on type 2 diabetes incidence and cardiovascular risk factors in both eligible and non-eligible patients, indicating that eligibility criteria for bariatric surgery may need to be revised and not based primarily on body mass index. Bariatric surgery also reduces the risk for overall cancer incidence, and specifically female cancers. Meanwhile, bariatric surgery increased the risk for alcohol use disorders, especially in gastric bypass operated patients, and patients should be carefully followed-up in order to identify such potential side effects. The *ITIH5* expression is increased in obesity, reduced after diet-induced weight loss, and is associated with variables of obesity and cardiovascular risk factors, suggesting that this gene is potentially involved in the molecular mechanisms linking obesity with morbidity.

**Keywords:** Obesity, bariatric surgery, vertical banded gastroplasty, gastric banding, roux-en-y gastric bypass, type 2 diabetes, cardiovascular risk factors, alcohol use disorders, cancer, *ITIH5*, adipose tissue

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